PATENT COOPERATION TREATY

RECEIVED

From the INTERNATIONAL SEARCHING AUTHORITY

PCT SEP 0 6 2005

ELI LILLY AND COMPANY

WOOD, Dan L. / P.O. Box 6288 Indianapolis IN 46206-6288 UNITED STATES OF AMERICA	NOTIFICATION OF TRANSMETER OF ISION THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION		
	(PCT Rule 44.1)		
	Date of mailing (day/month/year) 29/08/2005		
Applicant's or agent's file reference			
X-16648 V	FOR FURTHER ACTION See paragraphs 1 and 4 below		
International application No. PCT/US2005/005491	International filing date (day/month/year) 22/02/2005		
Applicant			
ELI LILLY AND COMPANY			
1. X The applicant is hereby notified that the international search Authority have been established and are transmitted herew	n report and the written opinion of the International Searching ith.		
Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claim	• • • • • • • • • • • • • • • • • • • •		
When? The time limit for filing such amendments is nor International Search Report; however, for more	mally 2 months from the date of transmittal of the details, see the notes on the accompanying sheet.		
Where? Directly to the International Bureau of WIPO, 34 1211 Geneva 20, Switzerland, Fa			
For more detailed instructions, see the notes on the acco	ompanying sheet.		
2. The applicant is hereby notified that no international search Article 17(2)(a) to that effect and the written opinion of the li			
3. With regard to the protest against payment of (an) addition	3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:		
	en transmitted to the International Bureau together with the stest and the decision thereon to the designated Offices. plicant will be notified as soon as a decision is made.		
4. Reminders			
Shortly after the expiration of 18 months from the priority date, the International Bureau. If the applicant wishes to avoid or postpone application, or of the priority claim, must reach the International Bufore the completion of the technical preparations for internation	publication, a notice of withdrawal of the international sureau as provided in Rules 90 <i>bis</i> .1 and 90 <i>bis</i> .3, respectively,		
The applicant may submit comments on an informal basis on the International Bureau. The International Bureau will send a copy of international preliminary examination report has been or is to be the public but not before the expiration of 30 months from the prior	of such comments to all designated Offices unless an established. These comments would also be made available to		
Within 19 months from the priority date, but only in respect of so examination must be filed if the applicant wishes to postpone the date (in some Offices even later); otherwise, the applicant must, acts for entry into the national phase before those designated Offices.	entry into the national phase until 30 months from the priority within 20 months from the priority date, perform the prescribed		
In respect of other designated Offices, the time limit of 30 month months.	s (or later) will apply even if no demand is filed within 19		
See the Annex to Form PCT/IB/301 and, for details about the apparate Guide, Volume II, National Chapters and the WIPO Internet site.			

Name and mailing address of the International Searching Authority

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Authorized officer

Tanja Rührmund

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been its filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

Notes to Form PCT/ISA/220 (first sheet) (January 1994)

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
 "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- 2 [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
 "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
 "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

Notes to Form PCT/ISA/220 (second sheet) (January 1994)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER	see Form PCT/ISA/220		
X-16648	ACTION	as well as, where applicable, item 5 below.		
International application No.	International filing date (day/montl	/year) (Earliest) Priority Date (day/month/year)		
PCT/US2005/005491	22/02/2005	25/02/2004		
	22/02/2005	25/02/2004		
Applicant				
ELI LILLY AND COMPANY				
EDI DIBDI AND COMPANI				
This International Search Report has been according to Article 18. A copy is being tra		ching Authority and is transmitted to the applicant		
This International Search Report consists	of a total of she	eets.		
l —	a copy of each prior art document of			
		·		
	international search was carried out ess otherwise indicated under this it	on the basis of the international application in the em.		
The international this Authority (Ru		of a translation of the international application furnished to		
		disclosed in the international application, see Box No. I.		
2. X Certain claims were fou	Certain claims were found unsearchable (See Box II).			
3. Unity of invention is lac	king (see Box III).			
4. With regard to the title,				
X the text is approved as su	bmitted by the applicant.			
the text has been establis	shed by this Authority to read as follo	ws:		
5. With regard to the abstract,	shmitted by the englished			
the text is approved as su	• • • • • • • • • • • • • • • • • • • •	sic Authority as it appears in Poy No. IV. The applicant		
		nis Authority as it appears in Box No. IV. The applicant ional search report, submit comments to this Authority.		
6. With regard to the drawings ,				
a. the figure of the drawings to be	published with the abstract is Figure	No		
as suggested by	the applicant.			
as selected by th	is Authority, because the applicant f	ailed to suggest a figure.		
as selected by th	is Authority, because this figure bett	er characterizes the invention.		
b. none of the figures is to b	e published with the abstract.			

INTERNATIONAL SEARCH REPORT

International Application No PCT/US2005/005491

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D295/12 C07D295/08 C07D295/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, PAJ, WPI Data

DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 22 April 2001 (2001-04-22), XP002340343 retrieved from STN	Relevant to claim No	
CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 22 April 2001 (2001-04-22), XP002340343 retrieved from STN	1,8	
Database accession no. 1955:56623 abstract & H. I. FUJIMURA ET AL.: "Syntheses and pharmacological action of Tetralin	1,8	
derivatives" YAKUGAKU ZASSHI - JOURNAL OF THE PHARMACEUTICAL SOCIETY OF JAPAN, no. 74, 1954, pages 954-956, JP; NIHON YAKUGAKKAI, TOKYO,		
FR 1 494 630 A (SANDOZ S. A) 8 September 1967 (1967-09-08) page 1, column 2, paragraph 2	1	
	& H. I. FUJIMURA ET AL.: "Syntheses and pharmacological action of Tetralin derivatives" YAKUGAKU ZASSHI - JOURNAL OF THE PHARMACEUTICAL SOCIETY OF JAPAN, no. 74, 1954, pages 954-956, JP; NIHON YAKUGAKKAI, TOKYO, FR 1 494 630 A (SANDOZ S. A) 8 September 1967 (1967-09-08)	

Further documents are listed in the continuation of box C	Patent family members are listed in annex
 Special categories of cited documents "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed 	 'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention 'X' document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. '&' document member of the same patent family
Date of the actual completion of the international search 11 August 2005	Date of mailing of the international search report 29/08/2005
Name and mailing address of the ISA European Patent Office, P B 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel (+31-70) 340-2040, Tx 31 651 epo nl, Fax (+31-70) 340-3016	Authorized officer Hoepfner, W

5

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/005491

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	✓GB 840 358 A (THE BRITISH DRUG HOUSES LIMITED) 6 July 1960 (1960-07-06) example 17	1
A	LIMITED) 6 July 1960 (1960-07-06)	1-15

5

International application No. PCT/US2005/005491

INTERNATIONAL SEARCH REPORT

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Although claims 9-15 are directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged effects of the compound/composition.
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2005/005491

	nt document search report		Publication date		Patent family member(s)		Publication date	İ
FR 1	494630	Α	08-09-1967	СН	457404	A	15-06-1968	
				ΑT	267498	В	27-12-1968	
				ΑT	268240	В	10-02-1969	
				ΑT	268241	В	10-02-1969	
				BE	687490	Α	28-03-1967	
				FR	6071	M	27-05-1968	!
				NL	6613360	Α	31-03-1967	
GB 8	40358	Α	06-07-1960	NONE				
EP 0	 375297	Α	27-06-1990	US	4902691	 A	20-02-1990	
				AU	621432		12-03-1992	
				AU	4675189	Α	21-06-1990	
				CA	2005506	A1	19-06-1990	
				CN	1043715	A,C	11-07-1990	
				DK	632189	Α	20-06-1990	
				EP	0375297	A2	27-06-1990	
				ΗÜ	52499	A2	28-07-1990	
				JP	2218682	Α	31-08-1990	
				MX	164891	В	30-09-1992	
				NZ	231774	Α	26-04-1991	
				PH	26522		07-08-1992	
				PT	92594	A,B	29-06-1990	
				ZA	8909580	Λ	28-08-1991	



PATENT COOPERATION TREATY

INTERNATIONAL SEARCHING AUTHORITY

То:				PCT	
see form PCT/ISA/220			INTERNATION (F	TEN OPINION OF THE NAL SEARCHING AUTHORITY PCT Rule 43.bis.1) NOV 2005 25 DEC 2005	
	cant's or agent's file reference form PCT/ISA/220		FOR FURTHER ACTION See paragraph 2 below		
	national application No. I/US2005/005491	International filing date (d. 22.02.2005	ay/month/year)	Priority date (day/month/year) 25.02.2004	
i	national Patent Classification (IPC) or I D295/12, C07D295/08, C07D2		and IPC		
Appl EL1					
1. This opinion contains indications relating to the following items: Box No. Basis of the opinion				usually be considered to be a lowever, this does not apply where chosen IPEA has notifed the tional Searching Authority PEA, the applicant is invited to nts, before the expiration of three	
Nam	e and mailing address of the ISA		Authorized Officer		

European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840

Hoepfner, W

Telephone No. +49 30 25901-337



WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US2005/005491

_	Box N	lo. I Basis of the opinion
1.		egard to the language , this opinion has been established on the basis of the international application in nguage in which it was filed, unless otherwise indicated under this item.
	la	his opinion has been established on the basis of a translation from the original language into the following nguage , which is the language of a translation furnished for the purposes of international search under Rules 12.3 and 23.1(b)).
2.		egard to any nucleotide and/or amino acid sequence disclosed in the international application and sary to the claimed invention, this opinion has been established on the basis of:
	a. type	e of material:
		a sequence listing
		table(s) related to the sequence listing
	b. forn	nat of material:
		in written format
		in computer readable form
	c. time	e of filing/furnishing:
		contained in the international application as filed.
		filed together with the international application in computer readable form.
		furnished subsequently to this Authority for the purposes of search.
3.	h: Co	addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto as been filed or furnished, the required statements that the information in the subsequent or additional opies is identical to that in the application as filed or does not go beyond the application as filed, as oppropriate, were furnished.
4.	Additio	onal comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US2005/005491

	Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability				
	The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:				
	the entire international applicat	ion,			
\boxtimes	claims Nos. 9-15 (w.r.t. industrial applicability)				
bed	cause:				
\boxtimes	the said international application, or the said claims Nos. 9-15 relate to the following subject matter which does not require an international preliminary examination (specify):				
	see separate sheet				
	the description, claims or drawings (indicate particular elements below) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):				
	the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.				
	no international search report has been established for the whole application or for said claims Nos.				
	the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:				
	the written form		has not been furnished		
			does not comply with the standard		
	the computer readable form		has not been furnished		
			does not comply with the standard		
	the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.				
	See separate sheet for further details				

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Yes: Claims 2-7,9-15 Novelty (N)

> Claims No:

1,8

Inventive step (IS) Yes: Claims 2-7,9-15

> No: Claims 1,8

Industrial applicability (IA) Yes: Claims 1-8

No: Claims

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 9-15 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- D1: DATABASE CAPLUS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 22 April 2001 (2001-04-22), XP002340343 retrieved from STN Database accession no. 1955:56623
- D2: FR-A-1 494 630 (SANDOZ S. A) 8 September 1967 (1967-09-08)
- D3: GB 840 358 A (THE BRITISH DRUG HOUSES LIMITED) 6 July 1960 (1960-07-06)
- D4: EP-A-0 375 297 (ELI LILLY AND COMPANY) 27 June 1990 (1990-06-27)

Novelty

The document D1 discloses N,N-diethyl-5,6,7,8-tetrahydro-2-naphthamide and its pharmaceutical use.

The document D2 discloses N-methyl-5,6,7,8-tetrahydro-2-naphthamine.

The document D3 discloses N-[2-(5,6,7,8-tetrahydronaphthyl)methyl]-piperazine.

All documents are silent on the medical use of their compounds in the treatment of obesity or other H3R-related diseases.

However, in view of these documents, the ISA fails to acknowledge novelty for the subjectmatter of present independent claims 1 and 8.

Inventive step

The document D4 is deemed closest prior art for the remaining novel subject-matter, since it addresses compounds suitable for the treatment of serotonin-receptor related diseases such as schizophrenia, sleep or appetite disorders (see page 1, lines 10, 11; page 1, Formula I; page 10, line 19).

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

PCT/US2005/005491

The distinguishing feature between the novel subject-matter and D4 is to be seen in the particular chemical structure of the compounds underlying the said novel subject-matter.

In the absence of any evidence for an unexpected technical effect linked to this feature, the objective problem underlying the novel subject-matter can merely be seen as the provision of further compounds suitable for the preparation of medicaments for the treatment of eating disorders.

The claimed solution to this very general problem was the provision of the particular compounds according to present claims 2-7.

However, since this solution was not derivable from the prior art on file, either read alone or in combination, the presence of inventive step has to be acknowledged for the remaining novel subject-matter, even in the absence of a technical effect.

Industrial applicability

There is no doubt that the subject-matter of the present claims 1-7 is industrially applicable.

However, for the assessment of the present claims ... on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.